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AMINOBENZIMIDAZOLE

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The invention concerns a new class of organic compounds, which can be called substituted Benzimidazole, and in particular such substituted Benzimidazole, which carry in the 1-Stellung a Amino or a substituted amino group, as well as procedure for the production of these compounds. The new compounds are usable as Anthelmintika and as fungicides.

The subject of the invention are substituted Benzimidazole of the general formula

I

in the R2 aryl, Orthohalogenaryl, an heteroaromatic group with 1 to 3 nitrogen and/or oxygen and/or sulfur atoms as Heteroatome or the group

in that R1 Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, AminoAlkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic group with 1 to 3 nitrogen and/or oxygen and/or sulfur atoms as Heteroatomen and X oxygen or sulfur is,

R5 and R6 hydrogen, halogen, niedrAlkyiamino, Di-loweralkylamino or the group

in that R1 and X the meaning indicated above have, are, are, under the condition that, if R5 and R6 are not halogen atoms at least R5 or R6 is hydrogen,
Alkanoyl, Carboxy loweralkanoyl or benzyle are, under the condition that only one of the groups of R3 and Alkanoyl or Carboxy loweralkanoyl is, and R3 and R4 together the group

Alkyl, Phenyl, Carboxy, Carboxy Alkanoyl is,

and the pharmaceutical acceptable acid addition salts and the pharmaceutical acceptable

alkali, alkaline-earth and amine salts of these compounds, if one of the groups of R7 and R8 or both groups of Carboxygroup are.

With the definition of the symbols the designations aryl and Aryloxy, aryl and Aryloxygroup, like Phenyl, are to cover R1 to R8 Naphthyl, Phenoxy and Naphthyloxy. AlkylAlkoxy are to cover geradkettige and verzweigtkettige alkyl, Alkylthio and alkoxy groups with 1 to 6 carbon atoms in the alkyl, Alkylthio or Alkoxyanteil, for example methyl, Xthyl, Isopropyl, Hexyl, Propylthio, Butylthio, Pentylthio, Methoxy, Äthoxy, Isopropoxy, Hexyloxy and such. The expressions Cyclo loweralkyl and Cyclo loweralkoxy are to cover Cycloalkyl and Cycloalkoxygroup with 4 to 8 carbon atoms, as for example Cyciobutyl, cyclohexyl, Cyclopentoxy, Cycloheptyloxy, Cyclooctyloxy and such. The designations Alkanoyl and Carboxy loweralkanoyl are to cover geradkettige and verzweigtkettige Alkanoyl and Carboxyalkanoylgroup with 1 to 6 carbon atoms, for example acetyl, Malonoyl, tri fluorine acetyl, Propionyl, Butyryl, Succinoyl and such. Those. Designation halogen covers fluorine, chlorine, bromine and iodine. The designations alkali and alkaline-earth salt are for example the lithium, sodium, potassium, cesium, calcium, magnesium, Carium and strontium salt cover. Pharmaceutical acceptable amine salts cover those from amines, like ammonia, ethanol amine, Diäthanolamin, Guanidin, arginin, Lysin, ethylen diamine, Piperazin and Morpholin. Pharmaceutical acceptable acid salts cover those inorganic and organic acids, like hydrochloric acid, lactic acid, Capronacid, asparagine acid, glow amine acid, citric acid and tartaric acid. Finally the designation heteroaromatic group heteroaromatic groups with a Heteroatom is in the Ringstruktur, like Thienyl, Furyl, Pyrryl; Pyridyl, Cumarinyl and Thiocumarinyl; heteroaromatic groups with two Heteroatomen in the Ringstruktur, like Thiazolyl, Isothiazolyl, Pyrazolyl, Oxazolyl and Imidazolyl; and heteroaromatic groups with three Heteroatomen in the Ringstruktur, like Thiadiazolyl, cover.

The invention is based on the discovery that the 1-Aminobenzimidazole described above is usable as Anthelmintika and fungicides. The physiological effect of the Benzimidazole in accordance with the invention is guaranteed by laboratory tests. In addition it was found that the Benzimidazole in accordance with the invention a noticeably better water and/or Lipoidlöslichkeit as the 1-Desaminobenzimidazole, from which they are derived, have and from there from special value been, if the use of liquid preparations is desired or if for the delivery of the active substance of a water and/or a Lipoidlöslichkeit is substantial. Preparations, which contain the Benzimidazole in accordance with the invention as substantial active substance, can be used thus for the treatment and fight against

Helminthiasis and as fungicides.

The 1-Aminobenzimidazole in accordance with the invention, i.e. those the Benzimidazole described above, in which R3 and R4 are hydrogen, can be manufactured easily by direct Amination of the appropriate 1-Desaminobenzimidazols. Appropriately Amination in way accomplished that one a solution or a suspension of a Ausgangs-1-desaminobenzimidazols, which can carry unsubstituted its or one of the substituents R2, R5 and R6 defined above in a suitable organic solvent, like methanol, ethanol, hexane, acetone, Dimethylsulfoxyd, dimethylformamide and such, with a Aminationsmittel, like Hydroxylamin O sulfonacid or chlorine amine, in presence of a base, as alkali or alkaline-earth hydroxides, - alkene oxides or - carbonates convert. The conversion can be accomplished at ambient temperature or the reaction mixture can gewünschtenfalls weakly, for example up to a temperature of for instance 50°C, warms up to be left. The conversion is usually in 24 to 72 hours terminated, and which knows formed 1-Aminobenzimidazol after diluting the reaction mixture with ice water is filtered off. The product can be cleaned by recrystallizing according to usual methods. The Benzimidazole used for this Amination as raw materials is available or easily producible in procedures well-known described in the literature compounds and either in the trade.

If the Benzimidazol used in the conversion as raw material, described above, is unsubstituted or in the 5 - and the 6-Stellung same substituents carries, by the introduction of the amino group to the 1-Stellung the symmetry, the molecule one does not destroy, and only an appropriate 1-Aminobenzimidazol is received. If against it the Ausgangsbenzimidazol in the 5 - or the 6-Stellung is substituted, or if it in the 5 - and 6-Stellung not the same substituents carries, leads, as for the specialist understandable, the introduction of the amino group in the 1-Stellung to a destruction the symmetry of the Benzimidazolkerns, so that the conversion product in the form of an isomer mixture will receive. If for example a Benzimidazol such as 5-Isopropoxy-carbonylamino-2 (4 ' - thiazolyl) - benzimidazol one subjects to a Amination, as described above, then a mixture of 1-Amino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) becomes as product - benzimidazol and 1-Amino-6-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol receive. Individual isomers can be separated in usual way chromatographisch or by fractionated crystallization.

The 1-Aminobenzimidazolesind as Anthelmintika and fungicides, received in the procedure described above, usable, but cannot only be used also as intermediate compound for the

production of all remaining 1-substituierten Aminobenzimidazole in accordance with the invention. The Ausgangs-1-aminobenzimidazole used in the following the descriptive procedure can in all other respects unsubstituted be or possibly which of the substituents R2, R5 and R6 described above carry.

Around the 1-substituierten Aminobenzimidazole in accordance with the invention, in those the substituents R3 and/or R4 Alkyl or benzyle is to manufacture can a solution or a suspension of any desired Ausgangs-1-aminobenzimidazols in a suitable organic solvent, like methanol, ethanol, acetone, hexane, benzene and suchAlkyl or - benzyle halide (i.e. a chloride, an iodide or a bromide) in presence of a base, like alkali or alkaline-earth hydroxides, - alkene oxides or - carbonates, to be converted. The reaction mixture is usually agitated 24 to 96 hours, and the product is won by evaporation of the solvent. The raw product received as arrears can be cleaned in usual way by recrystallizing. Alkyl or - benzyle halide is used, then the appropriate 1-Mono-loweralkylamino (or 1-Monobenzylamino) becomes as product - benzimidazol receive. Alkyl or - benzyle halide per mol of 1-Aminobenzimidazol becomes the appropriate 1-Di-loweralkylamino (or 1-Dibenzylamino) - benzimidazol receive. Alternatively the 1-Di-loweralkylamino (or 1-Dibenzylamino) - benzimidazole can be manufactured, by one a 1-Mono-loweralkylamino (or 1-Monobenzyl) - benzimidazol in the way with a further mol, described above, Alkyl or - benzyle halide converts. This method must naturally used, if compounds, in which the substituents are different R3 and R4, are to be manufactured.

The 1-substituierten Aminobenzimidazole in accordance with the invention, in those the substituent R3 or R4 Alkanoyl or Carboxy loweralkanoyl is, can be manufactured, by one a suspension or a solution of any desired exit 1 aminobenzimidazols in a suitable organic solvent, like methanol, ethanol, Alkanoylhalogenid (i.e. an iodide, a bromide or a chloride) or a Säureanhydrid, like an anhydride of the Mesoxyl, glow acre, amber or Suberinacid and such, converts. The reaction mixture is usually agitated 2 to 72 hours with ambient temperature, and the product is then precipitated by addition by ice water from the reaction mixture. After filtering the raw product off, the cleaning can take place via recrystallizing in usual way. If as reaction participants niedrAlkane dicarbonic acid anhydrides to be used, is the substituent R3 or R4 Carboxy loweralkanoyl.

Those compounds in accordance with the invention, in those the substituents R3 and R4 together the group

form,

can be generally manufactured, by converting a desired Ausgangs-1-aminobenzimidazol in a suitable organic solvent, inclusively for example Alkanolen, like methanol, ethanol and isopropanol and hydrocarbons, like benzene, toluol, hexane and such, with an aldehyde or a Keton. Which kind the substituents are R7 and/or R8, depends naturally on the used aldehyde or Keton.

For example those compounds know R7 or R8 (however not both) in accordance with the invention, in those Alkyl or · Phenyl are, to be manufactured, by one the Ausgangs-1-aminobenzimidazol, with Alkyl aldehyde, like acetaldehyde, Propionylaldehyd, n-Butyraldehyd, Isobutyraldehyd, n-Valeraldehyd, n-Caproaldehyd and such, or with benzyle aldehyde converts. Examples of Benzimidazole received with such aldehydes are all those the above general formula I, with those the substituent in the 1-Stellung

one of the substituents indicated in table I is:

Table I

If compounds are to be manufactured, in those both substituents Alkyl or Phenyl is, must only in the above procedure uses aldehyde by an appropriate Alkanon, like acetone, Diäthylketon, Äthylmethylketon, methyl n propylketon, 2-Hexanon, 3-Hexanon, Acetophenon, Propiophenon and such, or Benzophenon, to be replaced. Examples of Benzimidazole received with such Ketonen are those the above general formula I with one of the substituents indicated in the following table

in the 1-Stellung:

Table II

Those Benzimidazole in accordance with the invention, in which one of the substituents R7 or R8 or both Carboxy or Carboxy lower - alkyl is, can are manufactured, by one the Ausgangs-1-aminobenzimidazol with a Keto loweralkan mono or - dicarbonic acid converts. So for example compounds can, in which either R7 or R8 Carboxy is, while the other one of these two substituents is hydrogen, is manufactured, by converting the Ausgangs-1-aminobenzimidazol with Glyoxylacid. Likewise compounds can, in those one of the remainders R7 or R8 Carboxy or Carboxy loweralkyl and the other hydrogen or niedrAlkyl is, to be manufactured, by using another suitable Keto loweralkan monocarbonacid in place of the Glyoxylacid. If the Carbonylgroup of the Ketoacid is located in the α-position, are either R7 or R8 Carboxy Alkyl. If the Carbonylgroup stands in another than the α-position and not at the finalconstant carbon atom, then either R7 or R8 is Carboxy loweralkyl and the other one of these substituents Alkyl. If the Carbonylgroup at the finalconstant carbon atom stands, either R7 or R8 is Carboxy loweralkyl and the other one of these remainders hydrogen. Examples of Ketoacidn, which can be used for the production of the compounds described above, are α-Ketopropionacid, α-Ketobutteracid, A-Ketovalerianacid, α-Ketocaprylacid, 3-Ketobutteracid, 3-Ketovalerianacid, 4-Ketovalerianacid, Formylessigacid, 3-Formylpropionacid and such Benzimidazole in accordance with the invention, in which both substituents are R7 and R8 Carboxy or Carboxy loweralkyl, can be manufactured, by Keto monocarbonacidn instead of indicated the above a Keto loweralkan dicarbonic acid, as for example Mesoxalacid (Ketomalonacid), Ketobernsteinacid, 2-Ketoglutaracid, 3-Ketoglutaracid, 3-Ketoadipinacid, 4-Ketopimelinacid, 4-Ketosuberinacid and, uses such. Examples of Benzimidazole, which are manufactured using such Ketoacidn, are those Benzimidazole of the above general formula I with a group

in the 1-Stellung in accordance with the following table III.

Table III

Benzimidazole in accordance with the invention, in those either R7 Alkanoyl and other hydrogen is, can be manufactured, by converting the Ausgangs-1-aminobenzimidazol with an α-Keto-loweralkyl-aldehyde, as for example α-Ketopropionaldehyd, α-Keto-n-butyraldehyd, α-Keto-n-valeraldehyd and such. Examples of Benzimidazole, which are manufactured using such α-Ketoaldehyds, are those Benzimidazole of the general formula I with a group

Indicated in the 1-Stellung, as in the following table IV.

Table IV

Appropriately the conversions of the Ausgangs-1-aminobenzimidazols with an aldehyde or a Keton are accomplished, by one a solution or a suspension of the 1-Aminobenzimidazols in a solvent, as one indicated the above, with which converts desired aldehyde or Keton at the return flow. The time necessary up to the completion of the conversion depends on the kind of the Ausgangs-1-aminobenzimidazols and the selected aldehyde or Ketons and can in the range from 1 to 72 hours lie. The raw product can be won, by filtering the reaction mixture off diluted and the precipitation. By cleaning by recrystallizing the desired product will receive.

Although everyone can be manufactured the Benzimidazole of the above general formula I in the procedures described above, it can prove as appropriate, for the production of those compounds in accordance with the invention, with those the substituent R5 or R6 a R1-Thiocarbonylaminogroup

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where R1 has the meaning delivered in compound with the general formula I, is, to use as raw material 1.5 - (or 1,6) - Diamino-R2-benzimidazol (whereby R2 has the meaning indicated in compound with the general formula I). It was found that the 1-Amino-5 (or 6) - carbonylamino-R2-benzimidazole of the general formula I (i.e. those compounds, in those

the substituent R5 or R6.eine group

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in that R1 the meaning indicated in compound with the general formula I has, which can be manufactured after one of the procedures described above, easily into the appropriate 1,5 (or 1,6) - Diamino-compound to be converted, if they are subjected to a hydrolysis by acid. The hydrolysis can be accomplished appropriately in the way that one the 1-Amino-5 used as parent compound (or 6) - carbonylamino-R2-benzimidazol at return flow temperature with concentrated hydrochloric acid shifts. The conversion is usually in a time of 4 to 24 hours terminated, and the 1,5 received in the form of the hydrochloride (or 1,6) - Diamino-R2-benzimidazol is separated from the reaction mixture and shifted with a base, in order to receive the desired free Diaminobenzimidazol.

If in the 1-Amino-5 used as raw material (or 6) - carbonylamino-R2-benzimidazol the Alkoxy, Cyclo loweralkoxy or Aryloxy is, then the hydrolysis can take place to appropriate 1.5 - or 1,6-Diaminobenzimidazol alternatively in the way that one shifts the raw material at ambient temperature with concentrated sulfuric acid. The hydrolysis is terminated in 1 to 4 hours, and which formed Diaminobenzimidazol can by diluting the reaction mixture with ice water and following additive from base will receive.

As mentioned, like descriptive above by hydrolysis received 1.5 - (or 1,6) - Diamino-R2-benzimidazole the not only physiologically actively, but can also appropriately as intermediate compounds for the production of that Benzimidazol of the general formula I, in those the substituent in the 5 - or 6-Stellung are R1-Thiocarbonylaminogroup

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in that R1 the meaning indicated in compound with the general formula I has) is, to be used. It was found that the Thiocarbonylaminogroup in the 5 - or 6-Stellung to be easily formed can, by one the Ausgangs-1,5 (or 1,6) - Diamino-R2-benzimidazol with a Thiocarbonylhalogenid the formula

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in that R1 the meaning indicated in compound with the general formula I has and X a

halogen, preferably a chlorine or a bromine is, converts. This conversion can be accomplished, by one the Ausgangs-1,5 (or 1,6) - Di-aminobenzimidazol with the appropriate R1-Thiocarbonylhalogenid at room temperature in a suitable organic solvent, as for example hexane, a benzene, an acetone, a Dichlormethan or a such, converts. The reaction mixture is agitated about 1 until approximately 4 hours at ambient temperature, and which insoluble hydraulic halide of the Ausgangs-1,5 (or 1,6) - Diaminobenzimidazols during the conversion forms, by the reaction mixture one filters off. By evaporation of the filtrate and following recrystallizing of the arrears the desired 1-Amino-5 (or 6) becomes - R1--thiocarbonylarnino-R2-benzimidazol receive. Alternatively and with advantage the above conversion in an organic amine can be accomplished as solvents, for example Pyridin, whereby the formation of the hydraulic halide of the Ausgangsdiaminobenzimidazols is void.

When further appropriate alternative for the synthesis of Benzimdazolen of the general formula became I with a R1 - Thiocarboxylaminogroup in the 5 - or 6-Stellung found that 1-Amino-5 (or 6) - aryloxy (preferably phenoxy) - thiocarbonylamino-R2-benzimidazole, manufactured as described above, a transesterification Alkanol or Cyclo loweralkanol to be converted, so that the appropriate 1-Amino-5 (or 6) - loweralkoxy (or cyclo loweralkoxy) - thiocarbonylamino-R2-benzimidazol is formed. This conversion can be accomplished in the way that one uses as raw material 1-Amino-5-aryloxythiocarbonylamino-R2-benzimidazol in presence of a base, like alkali or alkaline-earth hydroxideAlkanol or Cycloalkanol warms up. Cooking at the return flow preferably takes place for 12 to 24 hours, and the product can be won then by evaporation of the reaction mixture and usual recrystallizing.

Accordingly know by shifting of the 1-Amino-5 (or 6) - aryloxythiocarbonylamino-R2-benzimidazole with ammonia, a mono or Di-loweralkylamin or with aniline, Pyrrolidin, Piperidin, Morpholin or Piperazin the appropriate 1-Amino-5 (or 6) - R2-benzimidazole, in those the Thiocarbonylamino substituent Alkylamionothiocarbonylamino, Di-loweralkylamionothiocarbonylamino, Anilinothiocarbonylamino, Pyrrolidin, Thiocarbonylamino, Piperidinthiocarbonylamino, Morpholinothiocarbonylamino or Piperazinthiocarbonylamino is, to be manufactured. This conversion can be accomplished at ambient temperature, by one the Ausgangs-1-amino-5 (or 6) - aryloxythiocarbonylamino-R2-benzimidazol with ammonia or the desired amine in a suitable organic solvent, like acetone, benzene, Dioxan, acetonitrile or such, converts. The conversion is usually terminated in a time of 12 to 36 hours, and the product by evaporation of the solvent and following recrystallizing of the arrears will receive.

As mentioned, naturally everyone can be used the 1-Amino-5 described above (or 6) - R1-thiocarbonylamino-R2-benzimidazole for itself as Anthelmintikum or fungicide, or gewünschtenfalls, in order the 1-Aminogroup can be subjected to a further chemical conversion into any by the general formula the I covered substituted amino groups to transfer. The procedures which can be used for such transformations are descriptive in detail above.

As mentioned, the Benzimidazole forms addition salts with pharmaceutical acceptable acids in accordance with the invention. Also those Benzimidazole form salts with alkali metals, alkaline earth metals and pharmaceutical acceptable amines in accordance with the invention, in which one of the substituents R7 or R8 is a Carboxygroup or is both Carboxygroup. Many of these salts possess a larger water solubility than the Stammimidazole and are from there from special importance if water-soluble preparations are desired. These salts can be manufactured in usual procedures, for example by bringing afterwards the Stammbenzimdazol with the desired acid or base in contact and evaporates the reaction mixture and in usual way wins and cleans the salt.

Even if all Benzimidazole possesses anthelmintische and fungicides effect in accordance with the invention, the efficiency is nevertheless naturally different and depends among other things on the which is possible kind of application, whereby the kind of application depends again on the strength of the infestation with the organisms which can be fought. Generally the preferential Benzimidazole is in accordance with the invention those, in which R3 and R4 are hydrogen, as well as those, in those R3 and R4 together the group

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as well as in the R7 or R8 hydrogen and the other one of these remainders of Carboxy is, forms their alkali, alkaline-earth and amine salts, in particular the Diäthanolaminsalze. R2 is preferably Thiazolyl and the preferential substituents in the 5 - and/or 6-Stellung are hydrogen and the group

If X is oxygen, preferably is R1 Alkoxy, in particular Methoxy, Äthoxy or Isopropoxy, Phenyl or p-Fluorphenyl. Alkoxy, in particular Methoxy, Phenyl or Pyrrolidino.

If the Benzimidazole is used in accordance with the invention for the treatment and fight against Helminthiasis, then it is not of substantial importance, in which form they are given to the animal, and it can for the treatment of infected. Animals or animals for the one risk of infection, everyone exists to be used so far for this purpose used working method. If the Benzimidazol in a dry firm unit dosage is to be given, then it is usually given in the form by caps, Bolusen or tablets, which contain the desired quantity of Benzimidazol. Such dosage forms are manufactured, by one the active substance intimately and evenly with suitable feindispersen diluents, fillers, which decay favouring means and/or bonding agents, like strength, mixes lactose, talcum powder, magnesium stearate, Pflanzengummis and such. Such unit dosages can regarding their total weight as well as their content of Anthelminti active substance depending upon kind of the landlord animal which can be treated, which and kind of the infection and the weight of the landlord vary weight within wide limits. For large animals, like sheep, pigs and cattle, unit dosages up to 15 g, which contain 3 to 12 g Benzimidazol, can be used. Usually however unit dosages with a weight are preferred from 5 to 10 g, which contain 2 to 8 g Benzimidazol. Boluse just like smaller tablets contain different bonding agents and lubricants, and their production takes place in actually well-known way. Caps can be easily manufactured, by one the active substance with a diluent, like strength or lactose mixes, and the mixture into the cap fills.

If infected animals are to be treated with a liquid medicine, the 1-Äther and 1-Ester-benzimidazole are mixed in accordance with the invention with a Suspensionsmittel, like Bentonit, and the firm mixture is brought directly before the administration into water. Alternatively ready for use such drugs, like in the US-PS 2,918,403 described, can being used. Preferential ones liquid drugs - % at the Benzimidazol.

The Benzimidazole described here can be added also to the fodder of the animals or solved or suspended in the drinking water. For this usable preparations contain the Benzimidazol intimately in an inert carrier or diluent dispersed. By an inert carrier a carrier is to be understood, which does not have no harmful effect on animals reacted with the Benzimidazol and. Preferably a carrier is used, which is a component of the fodder or can be.

Suitable preparations are fodder additives, in which the active substance is present in relatively large quantities, and which can be added to the fodder either directly or after

inserted dilution or mixture. Examples of suitable carriers or diluents of such preparations are Schlempe (distillers' dried grains), corn starch, Citrusmehl, fermentation arrears, vermahlene oyster bowls, wheat bran, soluble molasses components (molasses solubles), ear of corn starch, 8ohnenmahlfutter (edible bean mii1 feed), Sojaschrot, zerstoßener lime and such the active Benzimidazole thoroughly in it carriers are dispersed, for example through meals, mixing, mixing or rolling over. Preparations, those about 5 to 50 - % Benzimidazol contain, of own particularly well as fodder additives.

Examples of fodder additives, which contain the Benzimidazole in accordance with the invention in a firm carrier dispersed, are:

These and other fodder additives are manufactured, by interfering evenly the Imidazol into the carrier.

Such additives are added to the fodder in such quantity that the finished fodder contains the Benzimidazol in the concentration wished for the treatment and fight against Helminthiasis. The desired concentration at active substance depends naturally on the factors mentioned above as well as on the used Benzimidazol. Usually the Benzimidazole is used in accordance with the invention however in concentrations between 0,5 and 2,0% in the fodder, in order to obtain the desired anthelmintische effect.

The Benzimidazole in accordance with the invention is effective fungicides on different areas of application. They can be used from there according to usual methods as fungicides for the protection of plants, grounds, fruits, seeds, fur work, wood, paints, textiles, Kosmetika, leathers, tobacco, cordage, paper, stuff, plastics, fuel materials, rubber, food and such.

The Benzimidazole can be used depending upon the intended kind of application in different preparations, i.e. firm, inclusively feindisperser powders and granulates, as well as liquid, like solutions, emulsions, suspensions, concentrates, emulsive concentrates, mixing into a paste with and such. I.e. fungicides containing the Benzimidazole in accordance with the invention as active substances. Means know still for example feindisperse dry or liquid diluents, stretching means, fillers, Conditioners and Exzipienten, inclusively different clay/tone, Diatomeenerde, talcum powder and such, or water and

different organic liquids, like lowmolecular Alkanole, beside these active substances for example ethanol or isopropanol, or kerosene, benzene, toluol and other petroleum destillate ion parliamentary groups or mixtures of it, contain. The quantity of active substance, which is contained in such means, depends to a large extent on the used Benzimidazol and the intended kind of application. Generally the means between approximately 1 and about 95% at the active Benzimidasol contain.

The Benzimidazole in accordance with the invention can be used also in combination with one another or with other fungicides materials together. For example the Benzimidazole with Sorbinacid or its salts, Propionacid or its salts, Mycostatin, Natriumdiacetat, Trichomycin, Amphotercin, Griseofluvin, Undecylenacid, chlorine China DOL, 5, 7-Di chlor-8-hydroxychinolin (Vioform), specified above, knows, sodium o phenylphenat, o-Phenylphenol, Biphenyl, chlorinated Phenolen, Natriumbenzoat, D hydraulic acetic acid and their salts or esters of p-Hydroxy-benzoic acid, as are mixed methyl and Propylester (Parabens), so that on use of suitable concentrations additional fungicides effects are obtained. Also the Benzimidazole in accordance with of the invention can naturally. together with effective antibacterial materials to be used, if the circumstances let this appear suitable, so that the effects of each of the two active substances are combined, for example if the means to be used there are, if the presence of bacteria leads despite apart from the harmful effect from Fungi to unwanted results. A combination of fungicidal and bactericidal means is for example with the production of germizider soaps, Kosmetika as well as appropriate in food, like beer, cheese or meat or with leather.

It was also found that the growth of different Fungi is obstructed or prevented, if one applies small quantity of the Benzimidazolen in accordance with the invention to the ground. Each medium is to be understood, be covered growth about plants supported, and thus for example humus, sand, dung, compost, artificially manufactured plant growth solutions and such by "ground". It was also found that the Benzimidazole is effective in accordance with the invention against Funguserkrankungen of plants and either by direct contact with the sheet work or systemically, by introducing them by the roots can be used.

The compounds in accordance with the invention are effective also against bacteria and Pflanzennematoden and can be used into suitable concentrations for the inhibition or prevention of the growth of these organisms.

As fungicides the Benzimidazole is usable in accordance with the invention also for the

inhibition of the growth of mould with fruits, like Citrusfrüchten. The active substance can be preferably used at any time before consumption and after the harvest. For example that can be used fungicide during the initial storage, before or after transport or during the concluding storage before consumption. The Benzimidazole can be applied for this purpose in different way, either directly on the fruit in the form of an emulsion, a solution, a suspension or such, or to the fruit container or the packing material. Suitable carriers for the active substance are waxes and other materials at present well-known for such a purpose.

The best kind of the execution of the invention is illustrated in the following examples.

Example 1

1-Amino-2 (4 ' - thiazolvl) - benzimidazol

A suspension of 100,5 g 2 (4 ' - Thiazolyl) - benzimidazol in 2 1 ethanol under agitating 700 ml 2,6m aqueous sodium hydroxide are added. 100 g Hydroxylamin o sulfonacid in individual portions are added to in such a way received solution, so that the reaction temperature between 40 and 50° remains. Therein further 300 ml 2,6m aqueous sodium hydroxide solution and 50 g hydroxyl o-sulfonacid are added like above. The mixture is agitated 3 days at ambient temperature, according to which the largest part of ethanol is evaporated. Separated by addition of water the product pleases, and washed with water. By recrystallizing from benzene/ethanol 1-Amino-2 (4 ' - thiazolyl) becomes - benzimidazol, F 53 to 155°C, receive.

Example 2

1-Amino-5 (or 6) - isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

A suspension of 21,6 g 5-Isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol in 500 ml under agitating a solution is added to ethanol by 20 g sodium hydroxide in 300 ml water. In individual portions 28.8 g Hydroxylamin o sulfonacid are added to the received solution. The mixture is agitated 20 to grant at ambient temperature, according to which again sodium hydroxide solution and Hydroxylamin o sulfonacid are added above as. After agitating for further 4 hours the mixture of 1-Amino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) becomes - benzimidazol and 1-Amino-6-isopropoxy-carbonylamino-2 (4 ' -

thiazolyl) - benzimidazol by addition of 1,2 1 ice water pleases, filtered off and with water washed. The isomers by fractionated crystallization are separated. One receives 1-Amino-5-isopropoxy-carbonylamino-2 (4 ' - thiazolyl) - benzimidazol from ethyl acetate, F 192 to 193°C, and 1-Amino-6-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol from benzene, F 199 to 201°C).

Example 3

1-Amino--5 (or 6) - benzamido-2 (4 ' - thiazolyl) - benzimidazol a suspension of 9,6 g 5-Benzamido-2 (4 ' - thiazolyl) - benzimidazol in 95 ml Dimethylsulfoxyd under agitating 50 ml 2,6n aqueous sodium hydroxide are added and then to 7.5 g Hydroxylamin o sulfonacid in individual portions, so that the temperature is held with for instance 60°c. After 1 hour further 25 ml 2.6 n becomes aqueous sodium hydroxide and afterwards 4.9 g Hydroxylamin o--sulfone acid added. The mixture is agitated 20 hours at ambient temperature and diluted then with 1,2 1 ice water, whereby the product in the form of a mixture of 1-Amino-5-benzamido-2 (4 ' - thiazolyl) - benzimidazol and 1-Amino-6-benzamido-2 (4 ' - thiazolyl) - benzimidazol fails. The separation that isomers takes place via fractionated crystallization from a mixture from 2 parts methanol and 1 part dichloromethane. One receives 1-Amino-5-benzamido-2 (4 ' - thiazolyl) - benzimidazol, F 193 to 194°C, and 1-Amino-6-benzamido-2 (4 ' - thiazolyl) - benzimidazol, F 226 to 228°C).

Example 4

1-Amino-2-methoxycarbonylaminobenzimidazol

Ml dimethylformamide under agitating 27.5 ml 50%-iges aqueous sodium hydroxide and afterwards 30 g Hydroxylamin o sulfonacid in individual portions are added to a suspension of 19,1 g 2-Methoxycarbonylaminobenzimidazol in 200, so that the reaction temperature between 40 and 50°C is held. The mixture is agitated 1 day at ambient temperature and diluted then with water, in order to precipitate the 1-Amino-2-methoxycarbonylaminobenzimidazol, which is then separated and washed with water.

Example 5

1,2-Diaminobenzimidazol

Ml water under agitating 15 g Hydroxylamin oesulfonacid are added to a solution of 13,3 g 2-Aminobenzimidazol and 100 ml 2,6n NaOH in 400. After 1 hour again 100 ml 2,6n NaOH and afterwards 15 g Hydroxylamin o sulfonacid are added. The mixture is agitated 22 hours at ambient temperature. Then the product is filtered off and washed with water. By recrystallizing from ethanol 1,2-Diamino-benzimidazol, will receive F 260 to 262°C.

As mentions above, everyone can the 1-Aminobenzimidazole in accordance with the invention, i.e. each compound of the general formula I, in the R3 and R4 hydrogen is, by direct Amination after Stamm-1-desaminobenzimidazols in the examples the 1 to 5 described procedures to be manufactured. The Ausgangs-1-desaminobenzimidazol can naturally in the 2, 5 - and 6-Stellung substituted or ursubstituiert to be, as indicated above.

Example 6

5-Isopropoxycarbonylamino-1-methylamino-2 (4 ' - thiazolyl) - benzimidazol

A solution of 3,17 g 5-Isopropoxycarbonylamino-2 (4 ' - thiazoly1) - benzimidazol, 0.69 g potassium carbonate and 1.42 g methyl iodide in 100 ml acetone one agitates 4 days at ambient temperature. The solvent is evaporated and the arrears are washed with water. One receives 5-Isopropoxycarbonylamino-1-methylamino-2 (4 ' - thiazolyl) - benzimidazol.

Example 7

1-Dimethylamino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

A suspension of 3,31 g 1-Methylamino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol, 0.69 g potassium carbonate and 1.42 g methyl iodide in 100 ml acetone 4 days at ambient temperature one agitates. The solvent is evaporated and the arrears are washed with water. One receives 1-Dirnethylamino-5-ispropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol.

If in the examples 6 and 7 in place of the methyl iodide an equivalent quantity of a benzyle halide, for example benzyle chloride, is used, then one receives 5-Isopropoxycarbonylamino-1-benzylamino-2 (4 ' - thiazolyl) - benzimidazol and 1-Dibenzylamino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol.

Example 8

1-Trifluoracetylamino-2 (4 ' - thiazolyl) - benzimidazol

A suspension of 2,01 g 2 (4 ' - Thiazolyl) - benzimidazol in 10 ml Pyridin to 2.1 g tri fluorine acetic anhydrid are added. The mixture is agitated 2 hours at ambient temperature, according to which the product pleases by diluting with ice water becomes. By recrystallizing methanol one receives 1-Trifluoracetylamino-2 (4 ' - thiazolyl) - benzimidazol, F 279 to 280°C.

Example 9

1-Succinylamino-2 (4 ' - thiazolyl) - benzimidazol

A mixture of 6,6 g 2 - (4 ' - Thiazolyl) - benzimidazol and 3.3 g succinic acid anhydride in 200 ml 3 days at the return flow one cooks for dichloromethane. The precipitated product is separated and recrystallized from a mixture from methanol and ether, whereby one pure 1-Succinylamino-2 (4 ' - thiazolyl) - benzimidazol, F 203 to 204°C, receives.

Example 10

1-Acetylamino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

A mixture of 3,17 g 1-Amino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol and 0.8 g acetyl chloride in 20 ml Pyridin 2 hours at ambient temperature is agitated, by addition of 100 ml ice water becomes the 1-Acetylamino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol pleases.

Example 11

1-Benzylidenamino-2 (4 ' - thiazolyl) - benzimidazol

A mixture of 6,5 g 1-Amino-2 (4 ' - thiazolyl) - benzimidazol, ml acetic acid in 150 ml benzene 3 days at the return flow is cooked for 3, 50 g Benzaldehyd and 4, whereby the drug along water in a case of water is collected. By diluting the reaction mixture with

petroleum gasoline one receives 1-Benzylidenamino-2 (4 ' - thiazolyl) - benzimidazol, F 134°C.

If in the procedure of example 11 in place of the Benzaldehyds and/or the 1-Amino-2 (4 ' - thiazolyl) - benzimidazols an equivalent quantity of any other desired aldehyde and/or an equivalent quantity of any desired 1-Aminobenzimidazol one uses, then those Benzimidazole become in accordance with the invention, in those the substituent into the 1-Stellung a group

Alkyl aldehyde or Benzaldehyds as reagent compounds to be received, in those Alkyl or Phenyl is. Usable reagents and products are indicated in the above table I.

, If in place of the Benzaldehyds and/or the 1-Amino-2 (4 ' - thiazolyl) - benzimidazols of example 11 an equivalent quantity of any desired Keton and/or an equivalent quantity of any desired 1-Amino-benzimidazol one uses, that Benzimidazole in accordance with the invention, in those R7 and R8 become accordingly Alkyl or Phenyl is received. Examples of reagents and products are arranged in the above table II.

Example 12

1-Carboxymethylenamino-5-isopropoxycarbonyiamino-2 (4 ' - thiazolyl) - benzimidazol

A mixture of 32 g 1-Amino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol and ml isopropanol 1 1/2 are cooked for 21 g Glyoxylacid hydrate in 650 hours at the return flow. The product crystallizes from the cooled reaction mixture, F 176°C.

If in the procedure of example 12 an equivalent quantity of 1-Amino-6-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol, 1-Amino-2 (4 ' - thiazolyl) - benzimidazol, 1-Amino-5-benzamido-2 (4 ' -, thiazolyl) - benzimidazol or 1-Amino-6-benzamido-2 (4 ' - thiazolyl) - benzirnidazol in place of the 1-Amino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazols one uses, then 1-Carboxymethylenamino-6-ispropoxycarbonylamino-2 (4 ' - thiazolyl) can - benzimidazol, F 199°C, 1-Carboxymethylenamino-2 (4 ' - thiazolyl) - benzimidazol, F 170 to 172°C, 5-Benzamido-1-carboxymethylenamino 2 - (4 ' - thiazolyl) - benzimidazol, F 160°G and/or 6-Benzamido-1-carboxymethylenamino-2 (4 ' - thiazolyl) - benzimidazol, F 191 to 192°C, to

be manufactured.

Example 13

1 [α (2-Carboxyäthyl) - α-carboxy] - propylidenamino-5-benzamido-2 (4 ' - thiazolyl) - benzimidazol

A mixture of 1,68 g 1-Amino-5-benzamido-2 (4 ' - thiazolyl) - benzimidazol, ml acetic acid in 55 ml benzene 1 day at the return flow is cooked for 0.87 g 4-Ketopimelinacid and 2, whereby the drug along water in a case of water is caught. The product fails when cooling, F 296 to 297°C.

Example 14

(A-γ-Dicarboxy) - propylidenamino-5-benzamido-2 (4 ' - thiazolyl) - benzimidazol

1.68 g 1-Amino-5-benzamido-2 (4 ' - thiazolyl) - benzimidazol, 0.73 g 2-Ketoglutaracid and 2 ml acetic acid with 55 ml benzene are mixed. The mixture is cooked 24 hours at the return flow, whereby the drug along water in a case of water is caught. The reaction mixture is cooled, and that product is filtered off, F 110°C.

If in the procedures of the examples 12, 13 or 14 of the Ketoacidn and/or Benzimidazole used there an equivalent quantity of any other desired Keto mono is used or - dicarbonic acid and/or an equivalent quantity of any other desired 1-Aminobenzimidazol, then those Benzimidazole know R7 in accordance with the invention, in those or R8 or both groups of R7 or R8 Carboxy or Carboxy loweralkyl are, to be manufactured. For this suitable reagents and the received products are indicated in the above table III. Also those Benzimidazole can do one in accordance with the invention, in those R7 and R niedr by use A-Keto-loweralkylaldehyds in place of in these examples used the KetoacidAlkanoyl is, to be received. Examples and reagents and products are arranged in table IV.

Example 15

1, 5-Diamino-2 (4 ' - thiazolyl) - benzimidazol

10 g 1-Amino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol under agitating

to 20 ml to concentrated sulfuric acid are added. After 1 hour the reaction mixture with ice is diluted and shifted with ammonia, whereby the product, will receive F 200 to 202°C.

Example 16

1,5-Diamino-2 (4 ' - thiazolyl) - benzimidazol

A suspension of 71 g 1-Amino-5-benzamldo-2 (4 ' - thiazolyl) - benzimidazol in 600 ml ml water 7 hours at the return flow one cooks for concentrated hydrochloric acid and 400. The solution is cooled; the hydrochloride is filtered off, suspended in water and shifted with ammonia, whereby the product, will receive F 200 to 202°C.

Example 17

1, 6-Diamino-2 4 ' - thiazolyl) - benzimidazol

The procedure of example 15 becomes using 1-Amino-6-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol employs, the 1-Amino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazols repeats, whereby the 1,6-Diamino-2--(4 ' - thiazolyl) - benzimidazol, to F 230 to 234°C, one receives.

Example 18

1, 6-Diamino-2 (4 ' - thiazolyl) - benzimidazol

If in the procedure of example 16 1-Amino-6-benzamido- (4 ' - thiazolyl) - benzimidazol in place of the 1-Amino-5-bentzamido-2 (4 ' - thiazolyl) - benzimidazols one uses and one cooks the mixture 18 hours at the return flow, then one receives 1,6-Diamino-2 (4 ' - thiazolyl) - benzimidazol, F 230 to 234°C.

Example 19

1-Amino-5-methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazo

A solution of 3,87 g Methoxythiocarbonylchlorid in 70 ml Dichlormethan becomes drop by drop under agitating a suspension of 7,93 g 1, 5-Diamino-2 (4 ' - thiazolyl) - benzimidazol

added in 250 ml Dichlormethan. The solution is agitated still 1 1/4 hours at ambient temperature. The insoluble hydrochloride of the 1,5-Diamino-2 (4 ' - thiazolyl) - benzimidazols one filters off, and the product by evaporation of the filtrate will receive. By recrystallizing from methanol one receives 1-Amino-5-methoxy-thiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol, F 200 to 201°C.

Example 20

1-Amino-6-methoxyhiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

In the procedure of example 19, however using 1,6-Diamino-2 (4 ' - thiazolyl) - benzimidazol in place of the 1,5-Isomer one receives 1-Amino-6-methoxythiocarbonylamfno-2 (4 ' - thiazolyl) - benzimidazol.

Example 21

1-Amino-5-phenoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

In the procedure of example 19, however using 1,617 g 1,5-Diamino-2 (4 ' - thiazolyl) - benzinidazol and 1.21 g Phenylthiocarbonylchlorid instead of the Methylthiocarbonylchlorids one receives by recrystallizing from Dichlormethan the 1-Amino-5-phenoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol, F 174 to 175°C.

Example 22
1-Amino-5-Phenoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

0.86 g Phenoxythiocarbonylchlorid become drop by drop under agitating a solution of 1,15 g 1,5-Diamino-2 (4 ' - thiazolyl) - benzimidazol added in 15 ml Pyridin. After 1 hour the solution with ice water is diluted. The product is filtered off and recrystallized from Dichlormethan, F 174 to 175°C.

Example 23

1-Amino-5-methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

A solution of 3,6 g 1-Amino-5-phenoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

and ml methanol 24 hours at the return flow one cooks for 20 mg Natriummethoxyd in 300. The product will receive F 200 to 201°C by evaporation of the solvent and recrystallizing the arrears from methanol.

Example 24

1-Amino-6-phenoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

In the procedure of example 21 or 22 becomes using the 1,6-Diamino-2 (4 ' - thiazolyl) - benzimidazols in place of the 1,5-Diaminoisomer the 1-Amino-6-phenoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol receive.

Example 25

1-Amino-5-cyclobutylenthioureido-2 (4 ' - thiazolyl) - benzimidazol

A mixture of 100 mg 1-Amino-5-phenoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol lp 102 mg Pyrrolidin in 9 ml to acetonitrile 24 hours at ambient temperature one lets stand. A small quantity solid is filtered off. The solvent ird evaporated, and the arrears becomes with ether rubbed. One receives the product, F 209 to 210°C.

Example 26

1-Amino-6-cyclobutylenthioureido-2 (4 ' - thiazolyl) - benzimidazol

In the procedure of example 25, however using 1-Amino-6-phenoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimdazol in place of the 1-Amino-5-phenoxythiocarbonylaminoisomer one receives the 1-Amino-6-cyclobutylenthioureido-2 (4 ' - thiazolyl) - benzimidazol.

Example 27

1-Carboxymethylenamino-5-methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol

A mixture of 1,14 g 1-Amino-5-methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol and ml ethanol 1 hour at the return flow is cooked for 0.666 g Glyoxylacidhydrat in 25. By addition of ether becomes the product pleases, F 195 to 197°C.

If as Ausgangsbenzimidazol in the procedure of example 27 1-Amino-6-methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol, 1-Amino-5-cyclobutylenthioureido-2 (4 ' - thiazolyl) - benzimidazol
or 1-Amino-6-cyclobutylenthioureido-2 (4 ' - thiazolyl) - benzimidazol one uses, then one receives 1-Carboxymethylenamino-6-methoxy-thiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol, 1-Carboxymethylenamino-5-cyclobutylenthiou reido-2 (4 ' - thiazolyl) - benzimidazol (F 172 to 174°C) and/or 1-Carboxymethylenamino-6-cyclobutylen-thioureido-2 (4 ' - thiazolyl) - benzimidazol.

Example 28

1-Carboxymethylenamino-5-methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol diäthanolaminsalz

A suspension of 6,4 g 1-Carboxymethylenamino-5-methoxy-thiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol in 50 ml methanol 19.6 ml to a solution, which contains 2.10 g Diäthanolamin, with methanol filled up to 20 ml, are added. After a clear solution is received, the product becomes by addition of 100 ml isopropanol pleases, F 146 to 147°C (Zers.).

Example 29

1-Carboxymethylenamino-5-methoxythlocarbonylamino-2 (4 ' - thiazoly1) - benzimidazol diäthanolaminsalz

In the procedure of example 28, however using an equivalent quantity of tri ethanol amine in place of the Diäthanolamins one receives the tri ethanol amine salt of the 1-Carboxymethylenamino-5-methoxythiocarbonylamino-2 (4 ' - thiazoly1) - benzimidazols, F 60°C (Zers.).

Example 30

1-Carboxymethylenamino-5-Isopropoxycarbonylamino-2 (4 ' - thiazoly1) - benzimidazol diäthanolaminsalz

A solution of 4,05 g Diäthanolamin in 85 ml methanol 12 g 1-Carboxymethylenamino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) become - benzimidazol added. After a solution is received, the salt becomes by addition of ether pleases, F 136°C.

In the procedure of example 30, however using 1-Carboxymethylenamino-2 (4 ' - thiazolyl) - benzimidazol, 1-Carboxymethylenamino-5-benzamido-2 (4 ' - thiazolyl) - benzimidazol or - - benzimidazol in place of the 1-Carboxymethylenamito-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazols one receives the Diäthanolaminsalz of the 1-Carboxymethylenamino-2 (10-thiazolyl) to Carboxymethylenamino-6-benzamido-2 (4 ' - thiazolyl) - benzimidazols, F 140 to 141°C, the Diäthanolaminsalz of the 1-Carboxymthylenamino-5-Benzamido-2 (4 ' - thiazolyl) - benzimidazols, F 173°C, and/or the Diäthanolaminsalz of the 1-Carboxymethylenamino-6-benzamido-2 (4 ' - thiazolyl) - benziedazols, F 220 to 222°C.

Example 31

1-Carboxymethylenamino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol sodium salt

A solution of 3,73 g 1-Carboxymethylenamino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol in 20 ml a solution is added to methanol by 0,54 g Natriummethoxyd in 10 ml methanol. After a solution is formed, the salt becomes by addition of ether pleases.

Example 32

1-Amino-5--isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol
Hydrochloride

A suspension of 3,20 g 1-Amino-5-isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol in 20 ml a mixture is added to methanol by 10 ml 1n hydrochloric acid in 10 ml methanol. The reaction mixture is agitated 1 hour at ambient temperature, and the salt becomes by addition of ether pleases.

Patent claims

1. Procedure for the production of a Benzimidazolsder general formula

in the R2 aryl, Orthohalogenaryl, an heteroaromatic group with 1 to 3 nitrogen and/or oxygen and/or sulfur atoms as Heteroatome or the group

in that g 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic group with 1 to 3 nitrogen and/or oxygen and/or sulfur atoms as Heteroatomen and X oxygen or sulfur is,

R5 and R6 hydrogen, halogen, lower Alkyl, lower Alkoxy, lower - Alkylthio, Phenyl, Halogenphenyl, Phenoxy, Phenylthio, Amino, lower Alkylamino, Di-loweralkylamino or the group

in that g 1 and X the meaning indicated above have, are, are characterized, under the condition that, if R5 and R6 are not halogen atoms at least R5 and R6 are hydrogen, thereby that one a compound of the general formula

in presence of a base with a reinforcing means converts.

2. Procedure for the production of a Benzimidazols of the general formula

in that

R2 aryl, Orthohalogenaryl, a remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen or the group

in that g 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, P rrrolldino, Piperidino, Morpholino, Piperazino or an heteroaromatic group with 1 to 3 nitrogen, oxygen or sulfur atoms as Heteroatomen is, and X oxygen or sulfur is;

R5 and R6 hydrogen, halogen, lower Alkyl, lower Alkoxy, lower Alkylthio, Phenyl, Halogenphenyl, Phenoxy, Phenylthio, Amino, lower Alkylamino, Di-loweralkylamino or the group

in that g 1 and X the meaning indicated above have, are, under the condition that, if R5 and R6 are not halogen atoms at least one of them is hydrogen, and

R3 and R4 hydrogen, lower Alkyl or benzyle is,

thereby characterized that one a compound of the general formula

with a compound of the formula

in the R9 lower Alkyl or benzyle and X halogen are, in presence of a base convert.

3. Procedure for the production of a Benzimidazols of the general formula

In that
R2 aryl, Orthohalogenaryl, an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen or the group

in that g 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen is and X oxygen or sulfur is,

R5 and R6 hydrogen, halogen, lower Alkyl, lower Alkoxy, lower Alkylthio, Phenyl, Halogenphenyl, Phenoxy, Phenylthio, Amino, lower Alkyl amines, Di-loweralkylamino or the group

in that g 1 and X the meaning credit indicated above, are, under the condition that, if R5 and R6 are not halogen atoms at least R5 and/or R6 are hydrogen, and

R3 and R4 hydrogen, lower Alkanoyl or Carboxy loweralkanoyl are, under the condition that only one of the remainders of R3 or R4 lower Alkanoyl or Carboxy loweralkanoyl is,

thereby characterized that one a compound of the general formula

with one lower Alkanoylhalogenid or one lower Alkanoyl anhydride converts.

4. Procedure for the production of a Benzimidazols of the general formula

in that

R2 aryl, Orthohalogenaryl, an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen or the group

in that g 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen is, and X oxygen or sulfur is,

R5 and R6 hydrogen, halogen, lower Alkyl, lower Alkoxy, lower Alkylthio, Phenyl, Halogenphenyl, Phenoxy, Phenylthio, Amino, lower Alkylamino, Di-loweralkylamino or the group

in that g 1 and X the meaning indicated above have, are, under the condition that, if R5 and R6 are not halogen atoms at least one of them is hydrogen, and

R7 and R8 hydrogen, lower Alkyl or Phenyl is marked, by the condition that only R7 or R8 is hydrogen, by that one a compound of the general formula

with one lower Alkyl aldehyde or one lower Alkanon converts.

5. Procedure for the production of a Benzimidazols of the general formula

in that

R2 aryl, Orthohalogenaryl, a heteroarornatischer remainder with 1 to 3 nitrogen, oxygen or sulfur atoms as Heteroatomen or the group

in that

G 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, PIperldino, Morpholino, Piperazino or an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen and X oxygen or sulfur is,

R5 and R6 hydrogen, halogen, lower Alkyl, lower Alkoxy, lower Alkylthio, Phenyl, Halogenphenyl, Phenoxy, Phenylthio, Amino, lower Alkylamino, Di-loweralkylamino or the group

in that

G 1 and X the meaning indicated above have, are, under the condition that, if R5 and R6 are not halogen atoms at least R5 or R6 is hydrogen, and

R7 and R8 hydrogen, lower Alkyl, Carboxy, Carboxy loweralkyl it are, under the condition that only R7 or R8 hydrogen or lower Alkyl is,

thereby characterized that one a compound of the general formula

with a Keto mono or - dicarboxyi loweralkansäure converts.

6. Procedure for the production of a Benzimidazols of the general formula

in that

R2 aryl, Orthohalogenaryl, an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or Sehwefelatomen as Heteroatomen or the group

in that

G 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen and X oxygen or sulfur is,

R5 and R6 hydrogen, halogen, lower Alkyl, lower Alkoxy, lower Alkylthio, Phenyl, Halogenphenyl, Phenoxy, Phenylthio, Amino, lower Alkylamino, Di-loweralkylamino or the group

in that

G 1 and X the meaning indicated above have, are, under the condition that, if R5 and R6 are not halogen atoms at least R5 or R6 is hydrogen, and

R7 and R8 hydrogen-decay lower Alkanoyi are, under the condition that only R7 or R8 hydrogen or lower Alkanoyl is,

thereby characterized that one a compound of the general formula

with one α-Keto-loweralkylaldehyd converts.

7. Procedure for the production of a 1,5 (6) - Diaminobenzimidazols of the general formula

in that

R2 aryl, Orthohalogenaryl, an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen or the group

in that g 1 lower Alkyl, lower Alkoxy, Gyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkyiamino, Di-loweralkylamino, Anilino, Pyrrolidino, Pipörldino, Morpholin, Piperazino or a remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen is and X oxygen or sulfur is,

thereby characterized that one a 1-Amine-5 (6) - carbonyl aminobenzimidazol the general formula

in that g 1 and R2 the meaning indicated above have, with concentrated mineral acid convert.

8. Procedure for the production of a 1-Amino-5 (6) - thiocarbonyl aminobenzimidazols the general formula

in that

R2 aryl, Orthohalogenaryl, an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen or the group

is,

G 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic remainder with 1 to 3 nitrogen, oxygen

and/or sulfur atoms as Heteroatomen and X oxygen or sulfur is,

thereby characterized that one a 1,5 (6) - Diaminobenzimidazol of the general formula

with a Thiocarbonylhalogenid of the formula

in that g 1 the meaning indicated above has and X halogen is, converts.

9. Procedure for the production of a 1-Amino-5 (6) - thiocarbonyl aminobenzimidazols the general formula

in that

R2 aryl, Orthohalogenaryl, an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen or the group

in that g 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen and X oxygen or sulfur is, and

R10 lower Alkoxy or Cyclo loweralkoxy is,

thereby characterized that one a 1-Amino-5 (6) - aryloxy thiocarbonylaminobenzimidazol the general formula

with a compound of the formula R10 OH, in the R10 lower Alkyl or Cyclo loweralkyl is, converts.

10. Procedure for the production of a 1-Amino-5 (6) - thiocarbonyl aminobenzimidazols the general formula

in that

R2 aryl, Orthohalogenaryl, an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen or the group

in that g 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic remainder with 1 to 3 nitrogen, oxygen and/or sulfur atoms as Heteroatomen and X oxygen or sulfur is, and

R11 Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino or Piperazino is,

thereby characterized that one a 1-Amino-5 (6) - aryloxythiocarbonylaminobenzimidazol the general formula

with ammonia, a mono or Di-loweralkylamin, aniline, Pyrrolidin, Piperidin, Morpholin or Piperazin convert.

11. Benzimidazole of the general formula

in that

R2 aryl, Orthohalogenaryl, an heteroaromatic group with 1 to 3 nitrogen and/or oxygen and/or sulfur atoms as Heteroatome or the group

in that g 1 never Dr. alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, aryl, Aryloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino or an heteroaromatic group with 1 to 3 nitrogen and/or oxygen and/or sulfur atoms as Heteroatomen and X oxygen or sulfur is,

R5 and R6 hydrogen, halogen, lower Alkyl, lower Alkoxy, lower Alkylthio, Phenyl, Halogenphenyl, Phenoxy, Phenylthio, Amino, lower Alkylamino, Di-loweralkylamino or the group

in that g 1 and X the meaning indicated above have, are, are, under the condition that, if R5 and R6 are not halogen atoms at least R5 or R6 is hydrogen,

and R3 and R4 hydrogen, lower Alkyl, lower Alkanoyl, Carboxy loweralkanoyl or benzyle are, under the condition that only one of the groups of R3 and R4 lower Alkanoyl or Carboxy loweralkanoyl is, and R3 and R4 together the group

in the R7 and R8 hydrogen, lower Alkyl, Phenyl, Carboxy, Carboxy loweralkyl or lower Alkanoyl are, under the condition that only R7 or R8 hydrogen or lower Alkanoyl is,

and the pharmaceutical acceptable acid addition salts and the pharmaceutical acceptable alkali, alkaline-earth and amine salts of these compounds, if one of the groups of R7 and R8 or both groups of Carboxygruppen are.

12. Compound according to claim 11, in that

R2 Phenyl, Naphthyl, Orthohalogenphenyl, Orthohalogennaphthyl, Thienyl, Furyl,

Pyrryl, Pyridyl, Cumarinyl, Thiocumarinyl, Thiazolyl, Isothiazolyl, Pyrazolyl, Oxazolyl, Imidazolyl, Thiadiazolyl or the group

in that g 1 lower Alkyl, lower Alkoxy, Cyclo loweralkyl, Cyclo loweralkoxy, Phenyl, Naphthyl, Phenoxy, Naphthyloxy, Amino, lower Alkylamino, Di-loweralkylamino, Anilino, Pyrrolidino, Piperidino, Morpholino, Piperazino, Thienyl, Puryl, Pyrryl, Pyridyl, Cumarinyl, Thiocumarinyl, Thiazolyl, Isothiazolyl, Pyrazolyl, Oxazolyl, Imidazolyl or Thiadiazolyl is, is, and X oxygen or sulfur is, and

R5 and R6 hydrogen, halogen, lower Alkyl, lower Alkoxy, lower Alkylthio, Phenyl, Halogenphenyl, Phenoxy, Phenylthio, Amino, lower Alkylamino, Di-lowerAlkylamino or the group

in that g 1 and X the meaning indicated above have, are, under the condition that, if R5 and R6 are not halogen atoms at least R5 or R6 is hydrogen.

13. Compound according to claim 12, in that

R2 Thienyl, Puryl, Pyrryl, Pyridyl, Cumarinyl, Thiocumarinyl, Thiazolyl, Isothiazolyl, Pyrazolyl, Oxazolyl, Imidazolyl or Thiadiazolyl is and

R5 and R6 hydrogen or the group

are.

14. Compound according to claim 13, by characterized that R2 Thiazolyl and g 1 lower Alkoxy, Phenyl, p-Fluorphenyl or Pyrrolidino are.

15. Compound according to claim 14, in the R3 and R4 hydrogen or the group

in the R7 and R8 hydrogen or Carboxy are, are.

16. Compound according to claim 15, i.e. 1-Amino-2 (4 ' - thiazolyl) - benzimidazol.

17. Compound according to claim 15, i.e. 1-Amino-5 (6) - methoxy-carbonylamino-2 (4 ' - thiazolyl) - benzimidazo.

18. Compound according to claim 15, i.e. 1-Amino-5 (6) - äthoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol.

19. Compound according to claim 15, i.e. 1-Amino-5 (6) - isopropoxy-carbonylamino-2 (4 ' - thiazoly1) - benzimidazol.

20. Compound according to claim 15, i.e. 1-Amino-5 (6) - benzamido-2 (4 ' - thiazolyl) - benzimidazol.

21. Compound according to claim 15, i.e. 1-Amino-5 (6) - p-fluorbenzamido-2 (4 ' - thiazolyl) - benzimidazol.

22. Compound according to claim 15, i.e. 1-Amino-5 (6) - methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol.

23. Compound according to claim 15, i.e. 1-Amino-5 (6) - phenylthio-carbonylamino-2 (4 ' - thiazolyl) - benzimidazol.

24. Compound according to claim 15, i.e. 1-Amino-5 (6) - cyclobutylenthioureido-2 (4 ' - thiazolyl) - benzimidazol.

25. Compound according to claim 15, i.e. 1-Carboxymethylenamino-2 (4 ' - thiazolyl) - benzimidazol.

26. Compound according to claim 15, i.e. 1-Carboxyme thylenamino-5 (6) - isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol.

27. Compound according to claim 15, i.e. 1-Carboxymethylenamino-5 (6) - isopropoxycarbonylamino-2 (4 ' - thiazolyl) - benzimidazol diäthanolaminsalz.

28. Compound according to claim 15, i.e. 1-Carboxymethylenamino-5 (6) - benzamido-2 (4 ' - thiazolyl) - benzimidazol.

29. Compound according to claim 15, i.e. 1-Carboxymethylenamino-5 (6) - p-fluorbenzamido-2 (4 ' - thiazolyl) - benzimidazol.

30. Compound according to claim 15, i.e. 1-Carboxymethylenamino-5 (6) - phenylthiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol.

31. Compound according to claim 15, i.e. 1-Carboxymethylenamino-5 (6) - methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol.

32. Compound according to claim 15, i.e. 1-Carboxymethylenamino-5 (6) - methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol diäthanolaminsalz.

33. Compound according to claim 15, i.e. 1-Carboxymethylenamino-5 (6) - methoxythiocarbonylamino-2 (4 ' - thiazolyl) - benzimidazol triäthanolaminsalz.

34. Compound according to claim 15, i.e. 1-Carboxymethylenamino-5 (6) - cyclobutylenthioureido-2 (4 ' - thiazolyl) - benzimidazol.

35. Anthelminti means, thereby characterized that it contains a anthelmintisch effective quantity of one Benzimidazol in accordance with claim 11 and a pharmaceutical acceptable carrier.

36. Fungicide means, thereby characterized that it contains a fungicide effective quantity of a Benzimidazol in accordance with claim 11 and an inert carrier.